



PATENT
Atty. Dkt. No. PH-7038

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re appln. of: Wong)
U.S. Serial No.: 09/519,188)
Filed: 05/10/01) Examiner: Kim, V.
For: Treatment of Thrombosis by)
Combined Use of a Factor Xa)
Inhibitor and Aspirin, Tissue) Art Unit: 1614
Plasminogen Activator (TPA))
a GPIIb/IIIa Antagonist, Low)
Molecular Weight Heparin or)
Heparin)

Hon. Commissioner of
Patents and Trademarks
Washington, D.C. 20231

DECLARATION UNDER 37 CFR 1.131

1. This declaration is to establish completion of the invention in this application in the United States, at a date prior to March 23, 1999 which is the earliest effective date of the 102(e) references (U.S. Patent Nos. 5,886,191 and 6,060,491) that were cited by the Examiner.
2. The person making this declaration is the inventor.
3. The inventor conceived of the invention prior to the earliest effective date of said references cited by the Examiner and was diligent from prior to the effective date to a subsequent reduction to practice.
4. To establish the date of completion of the invention in this application, a photocopy of a notebook entry is submitted herewith as "EXHIBIT A" as evidence.
5. From this document it can be seen that the invention in this application was made prior to the earliest effective date of the references cited by the Examiner.

6. The inventor was diligent from the time of conception of the invention till the invention was actually reduced to practice and through the date the application was filed with the U.S. Patent Office.

7. This declaration is being submitted prior to final rejection.

8. As a person signing below I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole inventor: Pancras C. Wong
Pancras Wong

Inventor's signature: _____

November 7, 2001

Date: _____

Country of Citizenship: United States

Residence: 3227 Whiteman Road, Wilmington, DE 19808

Post Office Address: 3227 Whiteman Road, Wilmington, DE 19808



EXHIBIT A

SI

1590 43

DATE
SUBJECT

TO P.

Claim - Coadministration of two different with different sites of action would be synergistic and directed for thrombus formation for the treatment of thrombosis.

Claim OBJECT - Coadministration of an anticoagulant and an antiplatelet agent would be synergistic in preventing thrombus formation for the treatment of thrombosis.

Proposed studies (possible synergism)

- ① To examine a anti-thrombotic activity of coadministration of a fXa inhibitor such as SF 303 and a direct thrombin inhibitor such as XU 817 at their subthreshold doses. Heparin will also be examined.
- ② To examine possible synergistic anti-thrombotic activity of fXa inhibitor such as SF 303 and an antiplatelet agent such as GP IIb/IIIa inhibitor or thromboxane A₂ receptor inhibitor or thromboxane synthase inhibitor or a cyclooxygenase dependent platelet ~~inhibit~~ inhibitor such as aspirin or PGI_2 analog.
- ③ (Iloperat) To examine derivatives coadministration
- ④ To check GP IIb/IIIa inhibition and fXa inhibition in a guinea pig thrombosis model.
- ⑤ Another claim - fXa inhibitor such as SF 303 and direct thrombin inhibitor such as XU 817 would be useful as adjuncts to thrombolytic therapy with tPA. Using both a fXa inhibitor or a direct thrombin ~~inhibit~~ inhibitor together with tPA to induce thrombolysis would lower the dose of tPA needed to induce thrombolysis.

EXPERIMENTER
WITNESS

Panhas Wong
Gloria M. Zayed

DATE

DATE